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10/561,304	06/19/2006	Mark Del Borgo	087521-000000US	6537

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EXAMINER
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NIEBAUER, RONALD T

ART UNIT	PAPER NUMBER
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1654

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/561,304	<b>Applicant(s)</b> DEL BORGIO ET AL.	
	<b>Examiner</b> RONALD T. NIEBAUER	<b>Art Unit</b> 1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 07 August 2008.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,3,4,7,8,10-23,32,33 and 50-52 is/are pending in the application.
- 4a) Of the above claim(s) 4,7,8,10-23 and 50-52 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,3,32-33 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>8/7/08</u> .  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

Applicants amendments and arguments filed 8/7/08 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed is herein withdrawn.

Claims 1,3,7,10,14,15,17-19,32 have been amended. Claims 2,5-6,9,24-31,34-49 have been cancelled. Claims 50-52 have been added.

As discussed previously, Applicant's election with traverse of Group I (claims 1-23,32-33) in the reply filed on 2/13/08 is acknowledged. It is noted that applicant elected the peptide INSL3 (SEQ ID NO:7) as the peptide. Applicant also stated that they elected the A-chain of relaxin 1 and the reporter being a fluorescent reporter.

Since the election of species as stated in the written reply of 2/13/08 was unclear applicants representative Joseph Snyder was contacted on 3/10/08 as noted in the interview summary. Briefly, it was noted that the peptide INSL3 (SEQ ID NO:7) as identified in the written reply of 2/13/08 is a linear peptide, not a cyclic peptide as recited in claim 1. In other words, the sequence listing for SEQ ID NO:7 does not indicate that the peptide is a cyclic peptide. Further, it was noted that it was unclear which specific conjugate was elected and it was unclear which claims read on the elected invention. It was agreed that the peptide INSL3 (SEQ ID NO:7) would be searched as the elected peptide of the instant invention and that the peptide would be searched with respect to the claim limitations recited in claims 1 and 3. It was agreed that the species examined would be the peptide INSL3 (SEQ ID NO:7) as recited in claims 1 and 3 (i.e. no conjugate).

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As discussed above, the applicant agreed that the peptide INSL3 (SEQ ID NO:7) would be searched as the elected peptide of the instant invention and that the peptide would be searched with respect to the claim limitations recited in claims 1 and 3. With respect to newly added claims 50-52 it is noted that the peptide INSL3 (SEQ ID NO:7) has an amino acid sequence of PTPEMREKLCGHHFVRALVRVCGGPRWSTEA. Claims 50-52 are drawn to non-elected species. In particular, claims 50-51 are drawn to analogues that include the sequence TPCMREKLS... which is not found in SEQ ID NO:7. Claim 52 is drawn to analogues that include the sequence SCMEEVIK... which is not found in SEQ ID NO:7. In other words, since applicant has received an action on the merits for the originally presented invention and species, the invention and species have been constructively elected by original presentation on the merits (see MPEP section 821.03).

In the instant case the elected species was found in the prior art. As such the examination is limited to the generic claim and claims to the elected species (see MPEP section 803.02). In the instant case, claims 1,3,32-33 read on the elected species.

Claims 4,7-8,10-23,50-52 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention/species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 2/13/08.

Claims 1,3,32-33 are under consideration.

***Claim Rejections - 35 USC § 112***

Previously, claims were rejected under 112 2<sup>nd</sup>. Since claims have been amended an updated rejection appears below.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

**Claims 1,3,32-33** are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 and dependent claims 3,32-33 are drawn to monomeric cyclic peptide analogues. No specific definition has been set forth to identify analogues nor is there an art-recognized definition of analogue. Further, no specific degree or type of modification has been set forth for all the possible analogues. It is noted that a wherein clause appears in claim 1 that recites how the analogue is produced. However, such clause does not limit the analogues to a single particular feature. It is noted that Claim 3 states that the analogues are modified from a sequence set forth in SEQ ID NO:7. As such, the analogues do not necessarily have to share any common residues as SEQ ID NO:7 since any number of modifications can occur. The metes and bounds of the claims are unclear. The specific characteristics of an analogue are unclear. For example, since the specification teach amino acid substitutions (page 14 line 27-28 for example) it is unclear if a molecule that is cyclic and includes a conservative substitution for each and every amino acid of SEQ ID NO:7 would be considered an analogue of the instant invention although it shares no common residues. In other words, the term analogue can be read with more than one reasonable interpretation.

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Claim 1 has been amended to recite 'turn or loop moiety of the B-chain'. However, the metes and bounds of a turn or loop moiety is unclear. Turn and loop moieties are not defined by the claim and the specification does not provide a standard for ascertaining a turn or loop moiety. In other words, the distinguishing characteristics of a 'turn or loop moiety' have not been set forth. Further, it is unclear if 'turn' is meant to be a 'turn' within a specific element of the chain (for example a helix) or if 'turn' is meant to be the region between specific regions (for example between a helix and a beta strand) of a protein. Further, it is unclear if a moiety is meant to be a single molecule (for example hydrogen) or if moiety is meant to be something else such as an amino acid.

Claim 1 has been amended to recite 'alpha-helix or beta-strand carbon separation distance of less than six angstroms'. However, a standard for ascertaining such distance has not been set forth. It is unclear which specific 'carbon' residue is to be measured to determine the 'carbon separation' distance since an alpha-helix or beta-strand is likely to have more than one carbon. It is noted that the newly added claim limitation recites 'cross-linking the first and second amino acids'. It is unclear if the first and second amino acids are amino acids of a relaxin superfamily member protein or if the first and second amino acids are amino acids of an analogue of a relaxin superfamily member protein. It is noted that if the intent is to refer to a relaxin superfamily member then the cross-linking must occur via the naturally occurring residues. In other words it is unclear if the claims are to include modifications in which a cysteine residue for example is substituted for a residue of a relaxin superfamily member such that a disulfide cross-link can be formed. Taken together, the structure implied by the newly added wherein clause is unclear.

***Response to Arguments 112 2nd***

Since the claims have been amended, a new rejection adapted to the claims is recited above. Applicants arguments will be considered to the extent that they apply to the current rejection and claim set.

Applicants argue that the claims have been amended. Applicants argue that the specification teaches how to make cyclic peptides (Example 1 and 2 and pages 13-14) and that the sequences are shown in Figure 3. Applicants argue that binding data is demonstrated in Figure 1 and 2.

Applicant's arguments filed 8/7/08 have been fully considered but they are not persuasive.

Although applicants argue that the claims have been amended, the claim amendment does not clarify the previous issues and the amendment as discussed above actually introduces new issues.

Although applicant argues that the specification teaches how to make cyclic peptides and that the sequences are shown in Figure 3, limitations from the specification are not read into the claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Further, the examples and figures do not clearly define the metes and bounds of 'analogue' or 'turn or loop moiety' for example.

Although applicants argue that binding data is demonstrated in Figure 1 and 2, the instant claims are not drawn to binding data nor does binding data clarify the metes and bounds of the instant invention.

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Previously, claims were rejected under 112 1<sup>st</sup> written description. Since claims have been amended an updated rejection appears below.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

**Claims 1,3,32-33** are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

“To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that “the inventor invented the claimed invention.” Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (“[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.”). Thus, an applicant complies with the written description requirement “by describing the invention, with all its claimed limitations, not that which makes it obvious,” and by using “such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention.” Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.” Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

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“A written description of an invention involving a chemical genus, like a description of a chemical species, ‘requires a precise definition, such as by structure, formula, [or] chemical name,’ of the claimed subject matter sufficient to distinguish it from other materials.” *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) (“In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...”) *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is “not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.” MPEP § 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include “level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of

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such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient.” MPEP § 2163. While all of the factors have been considered, a sufficient amount for a *prima facie* case are discussed below.

In the instant case, the claims are drawn to cyclic peptide analogues. Claim 3 states that the analogue is modified from a sequence set forth in SEQ ID NO:7. Although unclear (see 112 2<sup>nd</sup> above) the claims have been interpreted broadly (see MPEP 2111) such that analogues include any amount of modifications. Although unclear (see 12 2<sup>nd</sup> above) the claims have been interpreted broadly with respect to the newly added wherein clause.

(1) *Level of skill and knowledge in the art:*

The level of skill in the art is high.

(2) *Partial structure:*

The claims are drawn to analogues. Claim 3 states that the analogue is modified from a sequence set forth in SEQ ID NO:7. Although unclear (see 112 2<sup>nd</sup> above) the claims have been interpreted broadly (see MPEP 2111) such that analogues include any amount of modifications.

Sections 0024,0069 of the specification (PGPub 20070004619) state that one or more amino acids within the peptide analogue sequence are optionally substituted. Section 0072 of the specification states that individual amino acids can be replaced by analogous structures, for example alkylmalonyl groups. Sections 0063-0068 of the specification state that a wide range of chemical linking groups can be used and a range of cyclization processes can be used.

[illegible]

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analogues. If there are substitutions with alkylmalonyl groups as discussed in section 0072 or if fusion compounds are considered the variability further increases. Hence, there is substantial variability in the genus.

Figure 3 shows 3 cyclic peptides (SEQ ID NOs: 11-13). However, the 3 examples provided are not representative of the genus (which includes well over  $20^{29}$  possible analogues).

Since there are a substantial variety of peptides possible within the genus, the examples do not constitute a representative number of species and do not sufficiently describe the genus claimed (see Gostelli above).

*(3) Physical and/or chemical properties and (4) Functional characteristics:*

Claim 1 describes the analogues as being of a B-chain of a relaxin superfamily member protein which binds to a biological target. Claim 1 refers to peptides in which the analogue is constrained. Section 0012 of the specification (PGPub 20070004619) states that ideally the analogues would include ligands, such as agonists, reverse agonists, partial agonists, mixed agonists/antagonists and full antagonists, which bind at the relaxin superfamily member receptors and initiate, inhibit, activate, or otherwise control, the biological activities of members of this protein superfamily. However, there is no disclosed correlation between structure and function for all of the analogues. Further, what constitutes an analogue is not clearly set forth. In particular, no common sequence or common core is taught for the analogs. It is noted that claim 3 recites a particular sequence but the claim is drawn to an analogue modified from that sequence. As such, there is no common core sequence. There is no teaching in the specification regarding what part of the structure can be varied while retaining the ability to bind a biological target. In particular, no common core sequence is taught. One of skill in the art would reasonably

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conclude that the disclosure fails to provide a representative number of species to describe the genus and that there is a lack of the knowledge in the art regarding which amino acids can vary to maintain the function and thus that the applicant was not in possession of the claimed genus.

*(5) Method of making the claimed invention:*

The specification (specifically example 1) describes the solid-phase synthesis of peptides, however the specification fail to describe the synthesis of a representative number of analogues.

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claim(s) 1,3,32-33 is/are broad and generic, with respect to all possible analogues encompassed by the claims. The possible structural variations are many. Although the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the peptides beyond those peptides specifically disclosed in the examples in the specification. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus. While having written description of peptides identified in the specification tables and/or examples, the specification does not provide sufficient descriptive support for the myriad of peptides embraced by the claims.

The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does “little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.”) Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and

does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

***Response to Arguments 112 written description***

Since the claims have been amended, a new rejection adapted to the claims is recited above. Applicants arguments will be considered to the extent that they apply to the current rejection and claim set.

Applicants argue that they are claiming the modification of 10 discrete molecules.

Applicants argue that the method of modification is well defined. Applicants argue that the specification teach how to make cyclic peptides and that analogues are shown in Figure 3 and that the written description requirement is met.

Applicant's arguments filed 8/7/08 have been fully considered but they are not persuasive.

[illegible]

Although Applicants argue that the method of modification is well defined, as discussed above (see 112 2<sup>nd</sup>) the new claim language introduced into claim 1 is unclear. Claim 1 has been amended to recite ‘turn or loop moiety of the B-chain’. However, the metes and bounds of a turn or loop moiety is unclear. Turn and loop moieties are not defined by the claim and the

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specification does not provide a standard for ascertaining a turn or loop moiety. In other words, the distinguishing characteristics of a 'turn or loop moiety' have not been set forth. Further, it is unclear if 'turn' is meant to be a 'turn' within a specific element of the chain (for example a helix) or if 'turn' is meant to be the region between specific regions (for example between a helix and a beta strand) of a protein. Further, it is unclear if a moiety is meant to be a single molecule (for example hydrogen) or if moiety is meant to be something more specific such as an amino acid.

Although Applicants argue that the specification teach how to make cyclic peptides and that analogues are shown in Figure 3 and that the written description requirement is met, the examples that applicants point to are not representative of the genus of 'analogues'. Figure 3 shows 3 cyclic peptides (SEQ ID NOs: 11-13). However, the 3 examples provided are not representative of the genus (which includes well over  $20^{29}$  possible analogues). Further, although the claims recite that the peptide 'binds to a biological target' there is no disclosed correlation between structure and function. There is no teaching in the specification regarding what part of the structure can be varied while retaining the ability to bind a biological target. In particular, no common core sequence is taught. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus and that there is a lack of the knowledge in the art regarding which amino acids can vary to maintain the function and thus that the applicant was not in possession of the claimed genus.

***Claim Rejections - 35 USC § 101***

Previously, claims were rejected under 101 on the same bases as cited below. Since claims have been amended an updated rejection appears below.

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

**Claims 1,3,32-33** are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

As discussed in detail in the 102 rejection Schwabe et al. (US 5,911,997) teach (Figure 1 and Figure 1 caption column 3 lines 43-49; claim 1) a peptide identified as the relaxin-like factor (RLF). The peptide includes the B-chain portion identified as SEQ ID NO:4 (i.e. PTPEMREKLCGHHFVRALVRVCGGPRWSTE A) which includes the primary sequence (without the disulfide bonds) identified as SEQ ID NO:7 of the instant invention. As shown in Figure 1 of Schwabe the B-chain of RLF is linked with the A-chain of RLF. In particular, residue 10 (i.e. Cys) and residue 22 (i.e. Cys) of the B-chain are linked to the A-chain. Together, residues 10-22 of the B chain of RLF form a cyclic structure with residues 11-24 of the A chain of RLF. In other words the sequence of the cyclic structure includes residues 10-22 of the B chain of RLF followed by residues 24-11 of the A chain of RLF (i.e. CGHHFVRALVRVCCLTLLDQQTCGSLC).

Although unclear (see 112 2<sup>nd</sup> above) the claims have been interpreted broadly (see MPEP 2111) such that analogues include any amount of modifications. Although unclear (see 12 2<sup>nd</sup> above) the claims have been interpreted broadly with respect to the newly added wherein clause.

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It is noted that claim 1 recites a monomeric cyclic peptide. As discussed above, Schwabe teach a cyclic structure that includes residues 10-22 of the B chain of RLF followed by residues 24-11 of the A chain of RLF (i.e. CGHHFVRALVRVCCLTLLDQQTCGSLC) (Figure 1), thus the peptide is cyclic. It is noted that Figure 1 depicts one specific structure therefore the peptide is monomeric. The peptide of Schwabe is an analog of SEQ ID NO:7 (a linear peptide) of the instant invention since the peptide of Schwabe includes disulfide bonds and cyclization thus meeting the limitations of claims 1,3 of the instant invention. It is noted that claim 1 states that the peptide modulates an activity of the biological target. Section 2112.01 of the MPEP states that products of identical chemical compositions can not have mutually exclusive properties. In the instant case, the peptide of Schwabe meet the claim limitations so the peptide necessarily has the claimed activity. It is noted that claim 1 recites ‘produced by...’. Section 2113 of the MPEP states that the structure implied by steps should be considered. Although unclear (see 112 2<sup>nd</sup>), since the peptide taught by Schwabe includes the modification of residues 10 and 22 of SEQ ID NO:7 and includes a cross-linking in which residues 10 and 22 of the B-chain are linked with residues 11-24 of the A chain the structure implied by the steps is met.

Schwabe teach that the relaxin-like factor (for example as shown in Figure 1) is from a human source (human Ley I-L) (column 3 lines 7-12 and column 2 lines 26-50).

There is no indication that the peptides of the current invention have been isolated or removed from a naturally occurring environment. The claimed subject matter therefore reads on a product of nature. Further, since Schwabe teach the peptides from a human source they are necessarily in a composition in the body that necessarily includes body fluids that act as carriers (see claims 32-33 of instant invention).

Although unclear (see 112 2<sup>nd</sup> above) the claims have been interpreted broadly (see MPEP 2111) such that analogues include any amount of modifications. Although unclear (see 12 2<sup>nd</sup> above) the claims have been interpreted broadly with respect to the newly added wherein clause.

### ***Response to Arguments 101***

Since the claims have been amended, a new rejection adapted to the claims is recited above. Applicants arguments will be considered to the extent that they apply to the current rejection and claim set.

Applicants argue that the claims have been amended. Applicants argue that the prior art does not teach a cyclic peptide.

Applicant's arguments filed 8/7/08 have been fully considered but they are not persuasive.

Although Applicants argue that the claims have been amended, such amendment does not indicate that the peptides of the current invention have been isolated or removed from a naturally occurring environment. Although Applicants argue that the prior art does not teach a cyclic peptide, as discussed in detail below residues 10-22 of the B chain of RLF form a cyclic structure with residues 11-24 of the A chain of RLF (Figure 1).

Further, it is noted that on page 12 (lines 12-13) of the reply that applicants states that the A and B chain naturally associate in vivo. Such statement provides support that the peptide is naturally occurring.

***Claim Rejections - 35 USC § 102***

Previously, claims were rejected under 102b using the reference cited below. Since claims have been amended an updated rejection appears below.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

**Claims 1,3,32-33** are rejected under 35 U.S.C. 102(b) as being anticipated by Schwabe et al. (US 5,911,997).

Schwabe et al. (US 5,911,997) teach (Figure 1 and Figure 1 caption column 3 lines 43-49; claim 1) a peptide identified as the relaxin-like factor (RLF). The peptide includes the B-chain portion identified as SEQ ID NO:4 (i.e. PTPEMREKLCGHHFVRALVRVCGGPRWSTE) which includes the primary sequence (without the disulfide bonds) identified as SEQ ID NO:7 of the instant invention. As shown in Figure 1 of Schwabe the B-chain of RLF is linked with the A-chain of RLF. In particular, residue 10 (i.e. Cys) and residue 22 (i.e. Cys) of the B-chain are linked to the A-chain. Together, residues 10-22 of the B chain of RLF form a cyclic structure with residues 11-24 of the A chain of RLF. In other words the sequence of the cyclic structure includes residues 10-22 of the B chain of RLF followed by residues 24-11 of the A chain of RLF (i.e. CGHHFVRALVRVCCLTLLDQQTCGSLC). Schwabe teach compositions of RLF (column 3

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line 7-12) and teach pharmaceutical compositions of RLF with carriers for example (column 8 lines 37-55) as recited in claim 32-33 of the instant invention.

Although unclear (see 112 2<sup>nd</sup> above) the claims have been interpreted broadly (see MPEP 2111) such that analogues include any amount of modifications. Although unclear (see 12 2<sup>nd</sup> above) the claims have been interpreted broadly with respect to the newly added wherein clause.

It is noted that claim 1 recites a monomeric cyclic peptide. As discussed above, Schwabe teach a cyclic structure that includes residues 10-22 of the B chain of RLF followed by residues 24-11 of the A chain of RLF (i.e. CGHHFVRALVRVCCLTLLDQQTCGSLC) (Figure 1), thus the peptide is cyclic. It is noted that Figure 1 depicts one specific structure therefore the peptide is monomeric. The peptide of Schwabe is an analog of SEQ ID NO:7 (a linear peptide) of the instant invention since the peptide of Schwabe includes disulfide bonds and cyclization thus meeting the limitations of claims 1,3 of the instant invention. It is noted that claim 1 states that the peptide modulates an activity of the biological target. Section 2112.01 of the MPEP states that products of identical chemical compositions can not have mutually exclusive properties. In the instant case, the peptide of Schwabe meet the claim limitations so the peptide necessarily has the claimed activity. It is noted that claim 1 recites 'produced by...'. Section 2113 of the MPEP states that the structure implied by steps should be considered. Although unclear (see 112 2<sup>nd</sup>), since the peptide taught by Schwabe includes the modification of residues 10 and 22 of SEQ ID NO:7 and includes a cross-linking in which residues 10 and 22 of the B-chain are linked with residues 11-24 of the A chain the structure implied by the steps is met.

***Response to Arguments 102***

Since the claims have been amended, a new rejection adapted to the claims using the same reference as previously is recited above. Applicants arguments will be considered to the extent that they apply to the current rejection and claim set.

Applicants argue that the background information refers to relaxin which is taught by Schwabe which applicants assert is not a monomeric cyclic peptide analogue. Applicants argue that interchain disulfide bonds are characteristic and well known as means of natural association. Applicants argue that Schwabe does not teach a modification of the B-chain.

Applicant's arguments filed 8/7/08 have been fully considered but they are not persuasive.

Although Applicants argue that the background information refers to relaxin which is taught by Schwabe which applicants assert is not a monomeric cyclic peptide analogue, as discussed above Schwabe teach a cyclic structure that includes residues 10-22 of the B chain of RLF followed by residues 24-11 of the A chain of RLF (i.e. CGHHFVRALVRVCCLTLLDQQTCGSLC) (Figure 1). Although applicant asserts that Scwabe does not meet the instant claims it is unclear as to what specific claim element is missing. It is noted that the claims are given the broadest reasonable interpretation. It is noted that the claims are drawn to cross-linking (see also the specification pages 13-14) but do not specify the specific type of cross-linking.

Although Applicants argue that interchain disulfide bonds are characteristic and well known as means of natural association, such argument supports the instant 101 rejection (see above) but does not distinguish the instant claims from the prior art.

Although Applicants argue that Schwabe does not teach a modification of the B-chain, it is noted that Figure 1 of Schwabe identifies the A chain and B chain. Further, as recited in instant claim 3, the peptide of Schwabe is an analog of SEQ ID NO:7 (a linear peptide) of the instant invention since the peptide of Schwabe includes disulfide bonds and cyclization which are modifications of SEQ ID NO:7. It is noted that SEQ ID NO:7 as provided in the sequence listing does not indicate disulfide bonds or cyclization. As such, the peptide of Schwabe is a modified from SEQ ID NO:7.

### ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to RONALD T. NIEBAUER whose telephone number is (571)270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Primary Examiner, Art Unit 1654

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Examiner, Art Unit 1654